Bioterrorism

A New Threat with Psychological and Social Sequelae

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Even in stable societies, destabilization or radical change can result from economic or environmental disaster, war, or any societal upheaval that leads to agitation, street disorder, and intimidation. Terrorism--a violent and often lethal form of intimidation--is intended to destabilize societies by causing fear, panic, social disorder, and economic chaos.[1] Individual or group terrorism can lead to guerrilla or civil war (as occurred recently in Peru, Zaire, and Rwanda). Even more ominous is government-sponsored terrorism (documented in Chile, Cambodia, Guatemala, Sierra Leone, East Timor, Yugoslavia, and Kosovo), which aims to suppress independence movements, reduce opposition to unpopular dictatorships, or eliminate indigenous peoples ("ethnic cleansing"). Terrorists often use conventional weapons (pistols and rifles) and explosive or thermal devices (bombs, mortars and missiles). Sometimes they use or threaten to use nonconventional (nuclear, biological, or chemical) weapons --"weapons of mass destruction." The effectiveness of any weapon can be assessed by *casualty generation* (the fraction of those exposed who are injured by a single use of the weapon) or *lethality* (the fraction who die). Traditionally, these measures have included only physical injury and illness, not the acute or chronic psychological sequelae. Nonconventional weapons appeal to terrorists because they can be highly lethal, can generate mass casualties, and, particularly, because they are likely to create fear and panic in those even marginally exposed.[1,2]

We use the word "Bioterrorism" to mean the terrorist use of microorganisms or toxins derived from microorganisms to produce death or disease in humans, animals, or plants.[3] Some 140 nations have renounced the overt use of biological warfare, but bioterrorism poses a real threat to public health and national security.[4-6] Potential bioterrorists include the mentally disturbed and psychotic, religious fanatics, political extremists, and organizations and nation states unwilling to abide by the Biological and Toxin Weapons Convention of 1972.

Biological weapons are characterized by high potency, low visibility, accessibility, and easy delivery. Inhaling one microgram of anthrax spores can be lethal, and once symptoms appear treatment is ineffective. This means a kilogram of anthrax spores could kill hundreds of thousands of people in a large city if delivered in optimal meteorological conditions. Similarly, 8 kg of botulinum toxin dispersed over 100 km^2 would, under ideal conditions, deliver a lethal dose to 50% of the population exposed. Botulism kills by paralyzing the respiratory muscles; it would be virtually impossible to provide ventilatory assistance and intensive care to large numbers of casualties.[7,8] Various hypothetical exposure scenarios for biological agents (Table 1) lead to similar catastrophic casualty estimates.[3,9-14]

Lethal amounts of biological agents are relatively easy to conceal, transport and disseminate. Unlike nuclear weapons or other advanced explosives, they can be dispersed from "crop duster" planes, backpack sprayers, humidifiers, or perfume atomizers. Recipes are readily available in public documents and on the Internet. Consequently, terrorists

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need only modest finances and basic familiarity with biology and engineering to produce effective biological weapons. Large organizations and rogue nations with access to large-scale fermentation, concentration, storage, and weapon facilities could cause major catastrophes.[5,7]

Table 1—Estimates of casualties produced by hypothetical biological attack*

Disease	Downwind Reach, km	No. Dead	No. Incapacitated
Rift Valley fever	1	400	35,000
Tick-borne encephalitis	1	9500	35,000
Typhus	5	19,000	85,000
Brucellosis	10	500	125,000
Q fever	>20	150	125,000
Tularemia	>20	30,000	125,000
Anthrax	>20	95,000	125,000

**Release of 50 kg of etiologic agent by aircraft along a 2-km line upwind of a population center of 500,000. Adapted from Christopher et al. Reprinted by permission.*

In 1984, 751 people in The Dalles, Oregon, contracted salmonellosis after members of a religious cult spread the bacteria on restaurant salad bars in an attempt to disrupt elections. In 1993, Canadian customs agents apprehended an Arkansas man who had four guns, 20,000 rounds of ammunition, and enough ricin (castor bean toxin) to kill 30 million people. Other extremists have been arrested in the US for possession of botulinum and ricin toxins. In 1995, an Ohio laboratory worker who belonged to a white supremacist group was arrested for ordering *Yersinia pestis,* the etiologic agent of bubonic plague. The bioterrorist threat to unsuspecting populations was demonstrated most dramatically when members of the Aum Shinrikyo cult attacked Japanese subway commuters in Matsumoto (1994) and Tokyo (1995) with the nerve gas sarin. More than a dozen people died, and nearly 6000 were injured. The cult was subsequently found to have an arsenal of anthrax bacilli, botulinum toxin, and VX nerve gas. Cult members had obtained Ebola virus from victims of an outbreak in Zaire. And recently we have learned of the chemical and biological weapons accumulated by Iraq.[1,10,12,15,16]

Human beings deeply fear infection and death from communicable disease.[17] The fear of contagion can be seen in the Biblical isolation of lepers; the plague pandemics of the Middle Ages; the cholera, yellow fever, and smallpox epidemics of the 19th century; and the influenza pandemics and polio epidemics of the early 20th century. Public health measures used to control the spread of communicable diseases include isolation and group quarantine. Quarantine not only diminishes secondary transmission, it provides a measure of psychological relief to those without illness who do not fully understand or accept the cause and mode of transmission of these diseases. Many of us remember the indelible images of iron lungs for polio victims or the sanatoria used to isolate and treat those with tuberculosis; more are acquainted with the psychosocial consequences of the recent AIDS pandemic, the rabies epizootic in the eastern US, Legionnaire's disease, toxic-shock syndrome, Lyme disease, the bovine variant of Creutzfeldt-Jacob disease, and other high profile diseases.

Today's news media often exacerbate public fear of contagion through reports that cite bogus "experts," distort facts, and exaggerate and sensationalize the public health risks of newly identified microbial hazards. Recent examples include media coverage of "flesh-eating bacteria" (necrotizing streptococcal infection), "mad cow disease," and "the cell from hell" (*Pfiesteria piscicida*), also called "fish AIDS" and "a waterborne Ebola virus." Emotions roused by such media coverage make it difficult for true experts in medicine, epidemiology, and infectious disease to bring reason to the situation.[17] The entertainment industry as well has capitalized on the public's fascination with microbes and the unknown, in movies ranging from the unbelievable transformation of an amoeba into "The Blob" (1958) to a somewhat more believable film, "Outbreak" (1995), which vividly depicts the public health and psychosocial sequelae of a fictional epidemic of Ebola virus hemorrhagic fever. Advertisement for this movie (viewed by tens of millions of people) shows a monkey with the caption "This animal carries a deadly virus . . . and the greatest medical crisis in the world is about to happen—try to remain calm."

The hyperbole of entertainment and media coverage, the public's innate fear of infection, and the fact that information disseminated by government agencies is sometimes skewed more toward what they want people to believe than what the facts indicate, led us to ponder the nature and history of biological terrorism, and to extrapolate (from data on natural and manmade disasters and on conventional terrorist attacks) the psychosocial consequences of a bioterrorist release of aerosolized anthrax spores, botulinum toxin, or other biological agents into a highly populated area.

We present an overview of preparedness for and responses to an attack, look at the anticipated psychological and social sequelae that would follow an attack, and summarize interventions that may help those evaluating and managing a bioterrorist crisis and may lessen acute and chronic psychological effects.

Table 2. Actual or proposed agents of terrorist attacks

Bacterial agents (diseases caused)
Bacillus anthracis (Anthrax)
Brucella spp (Brucellosis)
Clostridium perfringens (Gas gangrene)
Yersinia pestis (Plague)
Coxiella burnetti (Q fever)
Francisella tularensis (Tularemia)

Viral agents (diseases caused)
Variola virus (Smallpox, monkeypox, camelpox, etc.)
Togaviruses (Venezuelan/eastern/western encephalitis)
Various RNA viruses (Viral hemorrhagic fevers)
- Ebola virus
- Marburg virus
- Congo-Crimean hemorrhagic fever virus
- Yellow fever virus

Human rotavirus (Gastroenteritis)
Enterovirus 17 (Gastroenteritis, meningoencephalitis)

Toxins (mechanisms/effects)
Ricin (Pulmonary/gastrointestinal hemorrhage)
Tricothenes (Inhibition of DNA/protein synthesis)
Aflatoxin (Hepatotoxin, carcinogen)
Clostridium botulinum toxin (Neurotoxin, botulism-paralysis)
Staphylococcal enterotoxin B (Gastroenteritis)

Historical Perspective and Agents of Concern

Biological weapons have been used since the Middle Ages, when infected cadavers were catapulted over the walls of European cities and castles under siege. In America during the French and Indian War, the British supplied smallpox-virus-contaminated blankets to their Indian enemies. The advent of modern microbiology in the 19th century led to intensive efforts to identify and isolate specific pathogens suitable for use in war. During World War I, Germany mounted an ambitious, covert biological warfare (BW) program to infect livestock and contaminate animal feed destined for Allied Forces with *Bacillus anthracis* and *Burkholderia (Pseudomonas) mallei*, the etiologic agents of anthrax and glanders. The subsequent Geneva Protocol of 1925 prohibited the use of bacteriological weapons, but some signatories reserved the right to retaliate in kind if biological warfare was used against them. From 1932 until the end of World War II, Japan ran a large biological weapons research facility in occupied Manchuria, as a result of which prisoners and even entire cities were exposed to a variety of biological agents, including *B. anthracis*, *Neisseria meningitidis, Shigella spp, Salmonella spp, Vibrio cholera*, and *Yersinia pestis*. At least 10,000 prisoners died as a result of this experimentation, and thousands more died in field tests involving the contamination of water supplies and food with biological agents and the aerial dispersion of millions of fleas (propagated and fed on plague-infected rats) over Chinese cities. During and after World War II, many countries developed facilities for both offensive and defensive BW programs. By the late 1960s, the US biological arsenal included numerous bacterial pathogens, toxins and fungal plant pathogens (designed to induce crop failure and famine).[12]

During the 1950s and 1960s, the US military facilities at Fort Detrick, MD, and Pine Bluff, AR, conducted experiments on military and civilian human volunteers. They also studied dispersal of biological agents by exposing (surreptitiously) whole cities to aerosols of supposedly non-pathogenic bacteria such as *Serratia marcescens*. Between September 1950 and February 1951, 11 urinary tract infections (leading to one case of transient bacteremia and one death from endocarditis) followed the covert dispersal of *S. marcescens* over San Francisco. In 1976, a report in the *Washington Post* implied a causal association between such covert studies and illness (including pneumonia in Calhoun County, AL, and Key West, FL). Congressional hearings and independent scientific reviews never demonstrated a definite cause, but the temporal relationship between covert military operations and illness led to a public outcry that halted military experiments on unsuspecting populations.[12]

A 1970 World Health Organization report projecting staggering casualties of BW[18] led to the Biological Weapons Convention of 1972. This convention prohibited the development, possession, and stockpiling of pathogens or toxins in "quantities that have no justification for prophylactic, protective or other peaceful purposes," and prohibited the development of systems to disperse biological agents. Existing stocks of biological agents, delivery systems and equipment were to be destroyed, and the transfer of BW technology or expertise to other countries was prohibited. (Infractions by Iraq, one of the original signatory nations, represent a notable example of the treaty's limited effectiveness.)[10,12]

In 1969 and 1970, an executive order by President Nixon ended the US offensive BW program, and led to a US policy never to use biological weapons under any circumstances. Except for small quantities retained at Ft. Detrick, stocks of pathogens in the US biological arsenal were destroyed. The US Army Medical Research Institute of Infectious Diseases (USAMRIID) was established and military efforts were directed toward research on defense against BW (diagnostic tests, vaccines, antitoxins, toxoids, drugs and other specific therapies).[3,12]

It is not clear how well other countries have complied with disarmament, because verification is difficult. During the past 25 years, several accidents have involved BW agents. The most notable of these occurred in 1979, when the release

of anthrax spores from an offensive BW facility in Sverdlovsk, Soviet Union led to the death of 66 people.[19] More recently, the Iraqi development of a formidable offensive BW program, the Japanese subway attacks with sarin nerve gas, and a host of domestic threats have focused attention on BW and bioterrorism.

Biological agents and toxins capable of use as agents for terrorist acts are shown in Table 2.[1,2,7-10,20] Several of these (anthrax, botulinum toxin, and aflatoxin) were identified in the BW arsenals developed and made into weapons (some for missile deployment) by Iraq.[10] Aerosols of many viruses and bacteria are highly infectious and pose a public health threat, as illustrated by imported smallpox outbreaks that occurred in Canada (1962), Germany (1970), and Yugoslavia (1972), and by the 1979 Soviet anthrax epidemic.[21] Table 3, on pages 154-5, gives details on the infective dose, incubation period, clinical presentation, differential diagnosis, diagnostic assays, isolation precautions, chemotherapy, and chemoprophylaxis for the various agents.[8,9]

Preparedness and Response –An Overview

Bioterrorism may not provide the luxury of time for response on the part of those threatened. A bona-fide attack will pose daunting and immediate epidemiological and medical challenges. This means that the medical community, in concert with other agencies, must have planned and prepared adequately.

In addition to death and disability, the economic impact of a bioterrorist attack could be staggering. One model estimates that an attack with a relatively non-lethal agent such as *Brucella* could cost nearly $500 million/100,000 persons exposed, while a highly lethal agent like anthrax might cost more than $25 billion/100,000 persons exposed.[13] Well-coordinated prevention and post-attack contingency programs can markedly reduce panic, morbidity, mortality, and costs. Optimal outcomes require coordinated prior planning, preparation and training among government agencies (including public health agencies and laboratories), health care facilities, and the local civilian health care community.[4,6,13] We will need action by individuals with demonstrated expertise and leadership in medicine, epidemiology, infectious disease, pathology, molecular and microbiology (to identify specific strains of organisms), nursing, emergency medicine, military medicine, veterinary medicine, public health, mental health, law enforcement, and communications. All must work together to identify and contain the problem and limit the potential for catastrophe.[1,4,17,22]

Bioterrorism may have adverse psychological effects on responders as well as the public; if rescue and medical response efforts appear to be failing, social chaos may follow. It is critical to public confidence that the leaders of a response act as a cohesive unit, keeping focused on their mission while responding to basic human needs.[23] A scientific assessment of risks, coupled with timely and accurate communication by public officials and the media, will reduce adverse psychological sequelae. Real dialogue, neither exaggerating nor downplaying the risk, will help prevent panic and demoralization.[17]

Since a bioterrorist event could quickly overwhelm local and state response capabilities, a national response capability is needed. In 1995, President Clinton signed Presidential Decision Directive 39 (PDD-39), assigning lead responsibility for cases of domestic terrorism to the FBI. PDD-39 defines responsibilities and coordination among federal agencies. As with natural disasters, the Federal Emergency Management Agency (FEMA) will coordinate federal assistance to state and local governments. The Departments of Defense (DOD), Energy (DOE), Transportation (DOT), Agriculture (DOA), and Health and Human Services (DHHS), and the Environmental Protection Agency (EPA) will assist the FBI and FEMA as necessary. Responsibility for the emergency support of "health, medical, and health-related social services" is given to the US Public Health Service (PHS) within the DHHS. In the event of a chemical or biological terrorist event, the PHS Office of Emergency Preparedness is to implement and coordinate health and medical assistance. The Food and Drug Administration (FDA) is to procure and manage stockpiles of antidotes and pharmaceuticals.[24]

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The PHS has disaster medical assistance teams (DMATs) trained to deal with the special scenarios created by chemical and biological terrorism. These teams are designed to be deployed and on site within 12 hours of an event. If need be, the PHS can deliver direct medical care to disaster survivors through the National Disaster Medical System (NDMS), a system of 72 federal coordinating medical centers, which control 118,000 private-sector beds. Additional bed capacity is available at military hospitals, the US Department of Veterans Affairs and the DHHS. DHHS has created a specialized multi-agency (DHHS, DOD, DOE, and EPA) medical response team known as the Chemical-Biological Rapid Deployment Team (CBRDT). Led by the PHS and based in Washington, the CBRDT can be rapidly deployed as medical support for the on-scene manager of a terrorist incident.[24]

Because of the threat of domestic bioterrorism and our evident lack of preparedness, Congress, in 1996, passed the

Table 3 Summary of potential bioterrorism agents*

Disease (or Agent)	Infective Dose via Aerosol	Incubation Period	Diagnostic Samples (BSL)	Diagnostic Assay	Patient Isolation Procedures
Anthrax	8000-50,000 spores	1-5 days	Blood(BSL-2) Serology:ELISA	Gram Stain; Ag-ELISA	Standard precautions
Brucellosis	10-100 organisms	5-60 days	Blood, bone marrow; acute and convalescent sera (BSL-3)	Serology: agglutination Culture	Standard precautions Contact isolation if draining lesions present
Plague	100-500 organisms	2-3 days	Blood, sputum, lymph node aspirate (BSL 2/3)	Gram or Wright-Giemsa Stain; Ag-ELISA; Culture; Serology:ELISA, IFA	Pneumonic: droplet precautions until patient treated for 3 days
Q fever	1-10 organisms	10-40 days	Serum (BSL 2/3)	Serology:ELISA, IFA EM	Standard precautions
Tularemia	10-50 organisms	2-10 days	Blood, sputum, serum EM of tissue (BSL 2/3)	Culture; Serology: agglutination	Standard precautions
Smallpox	??10-100 organisms	7-17 days	Pharyngeal swab, scab material (BSL-4)	ELISA, PCR; virus isolation	Airborne precautions
Viral encephalitides	10-100 organisms	VEE 2-6 days EEE/WEE, 7-14 days	Serum: VEE (BSL-3) EEE/WEE (BSL-2)	Viral isolation Serology:ELISA hemagglutination inhibition	Standard precautions (mosquito control)
Viral Hemorrhagic fevers (VHF)	1-10 organisms	4-21 days	Serum, blood Most VHF (BSL-4) RVF, KHF, YF (BSL-3)	Virus isolation. Ag-ELISA; RT-PCR Serology:Ab-ELISA	Contact precautions; more for massive hemorrhage
Botulinum	0.001 μg/kg (Type A)	1-5 days	Nasal swab (possibly) (BSL-2)	Ag-ELISA mouse neutral	Standard precautions
Staphylococcal enterotoxin B	30 ng incapacitates, 1.7 μg kills	1-6 hours	Nasal swab, serum, urine (BSL-2)	Ag-ELISA Serology: Ab-ELISA	Standard precautions

Adapted from Franz et al; reprinted by permission. Information on diagnostics, medical management, and vaccines is available from the Commander, USAMRIID. Readers should consult product literature before administering drugs or vaccines.

Abbreviations used: BSL = biosafety level; Ag = antigen; Ab = antibody; ELISA = enzyme-linked immunosorbent assay; EM = electron microscopy; IFA = immunoflourescent assay; VEE = Venezuelan equine encephalitis, EEE = eastern equine encephalitis; WEE = western equine encephalitis; PCR = polymerase chain reaction; RT-PCR = reverse transcriptase-polymerase chain reaction

This page is a lateral continuation of Table 3. Pages 154-155 should be printed out and read side by side.

Chemotherapy	Chemoprophylaxis	Vaccine Availability	Comments
Cipro 400mg IV q 8-12 h or DCN 200 mg, then 100 mg IV q 8-12 h or Pen 2 million units IV q 2 h plus plus strep 30 mg/kg IM q d (or gent)	Cipro 500 mg PO bid x 4 wk if unvaccinated begin initial doses of vaccine DCN 100 mg PO bid x 4 wk plus vaccination	Michigan Biological Products Institute vaccine (licensed) 0.5 ml SC at 0, 2, 4 wk; 6, 12, 18 mo then annual boosters	Vaccine: boost annually if at risk Alternative Rx: gent, e-mycin,and CAPL
DCN 200 mg/d PO plus rifampin 600-900 mg/d PO x 6 wk	DCN and rifampin for 3 wk if inadvertently inoculated	No vaccine for human use	TMP-SMX may be used for rifampin, but up to 30% relapse
Strep 30 mg/kg IM bid x 10 d (or gent) or DCN 200 mg IV then 100 mg IV q 12 h x 10-14 d. CAPL 1 gm IV q 6 h x 10-14 d (indicated for plague meningitis)	TCN 500 mg PO qd x 7 d or DCN 100 mg PO q 12 h x 7 d	Greer inactivated vaccine (licensed): 1.0 mL, then 0.2 mL; booster at 1-3 and 3-6 mo	Boost at-risk 12, 18 mo & yearly. Plague vaccine does not protect against aerosol in animal studies. Alternative Rx: CAPL or TMP-SMX
TCN 500 mg PO q 6 h x 5-7 d DCN 100 mg PO q 12 hr x 5-7 d.	TCN or DCN for 5 d; start 8-12 days after exposure	IND 610-inactivated whole cell vaccine single 0.5 mL dose SC	Recommend skin test before vaccination
Strep 30 mg/kg IM q d x 10-14 d Gent 3-5 mg/kg/d x 10-14 d	DCN 100 mg PO q12 h or TCN 2 g/d PO x 14 d	Live attenuated vaccine (IND) by scarification	Culture difficult and potentially dangerous
Cidofovir (effective in vitro)	Vaccinia immune globulin 0.6 mL/kg IM (by day 3 after exposure; best within 1)	Calf lymph vaccinia vaccine; DOD cell- culture derived vaccine(IND): scarification	Pre- and postexposure vaccine recommended if >3 y since last vaccination
Supportive therapy; analgesics anticonvulsants as needed	NA	VEE: DOD TC-83 live attenuated vaccine (IND): 0.5 mL SC once; VEE: DOD C-84 (inactivated . TC-83) (IND): 0.5 mL SC for up to 3 doses; EEE/WEE inactivated (IND):EEE 0.5 mL SC at 0 & 28 d; WEE 0.5 mL At 0, 7, 28 d	TC-83 reactogenic in 20%; 20 % don't sero-convert; only effective against sub- types 1A, 1B, 1C Vaccine used for non-responders to TC-83. EEE and WEE inactivated vaccines poorly immunogenic; require multiple doses
Supportive therapy; Ribavirin for CCHF/arenaviruses 30 mg/kg IV, then 15 mg/kg q 6 h x 4 d, then 7.5 mg/kg q 8 h x 6 d. Passive antibody for AHF, BHF, CCHF, Lassa fever	NA	AHF Candid #1 vaccine (protection for BHF) (IND) RVF inactivated vaccine (IND)	Aggressively treat secondary infections and hypotension
DOD heptavalent antitoxin (Serotypes A-G) (IND): equine despeciated 10 mL IV;CDC Trivalent equine antitoxin for Serotypes A, B, E (licensed)	NA	DOD pentavalent toxoid for serotypes A-E (IND): SC at 0, 2, 12 wk, then yearly boosters	Skin test for hypersensitivity before giving equine antitoxin. Ventilatory assistance
Ventilatory support and supportive care	NA	No vaccine available	Vomiting and diarrhea if toxin swallowed

Cipro = Ciprofloxacin; DCN = doxycycline; TCN = tetracycline; pen = penicillin; strep = streptomycine; gent = gentamycin; e-mycin = erythromycin; CAPL = chloramphenicol; TMP-SMX = trimethoprin-sulfamethoxazole; IV = intravenous; IM = intramuscular; PO = by mouth; SC = subcutaneous; qd = each day; bid = twice a day; IND = Investigational New Drug; DOD = Department of Defense; NA = not available; KHF = Korean hemorrhagic fever; YF = yellow fever; RVF = Rift Valley fever; CCHF = Congo-Crimean hemorrhagic fever; AHF = Argentine hemorrhagic fever; BHF = Bolivian hemorrhagic fever.

Table 4. Contact agencies and phone numbers* for suspected bioterrorism incident or illness

NC Department of Health and Human Services (NCDHHS), Raleigh, NC
Division of Public Health, Epidemiology and Communicable Disease Section
General Communicable Disease Control Branch
919/733-3419

Centers for Disease Control and Prevention (CDC), Atlanta, GA
National Center for Environmental Health
Emergency Response Coordination Group
770/488-7100
US Army Medical Research Institute of Infectious Diseases (USAMRIID), Ft. Detrick, MD
Contact the Commander at 301/619-2833
Federal Bureau of Investigation (FBI), Charlotte, NC
704/377-9200
State Bureau of Investigation (SBI), Raleigh, NC
919/662-4500

** Available 24 hours a day*

Table 5. Diagnostic criteria for acute stress disorder*

A. The person has been exposed to a traumatic event characterized by both of the following:
   1. actual or threatened death or serious injury, or a threat to the physical integrity of self or others
   2. a response of intense fear, helplessness, or horror

B. Either during or after the event, the person has three or more of the following dissociative symptoms:
   1. a subjective sense of numbing, detachment, or absence of emotional responsiveness
   2. a reduction in awareness of his or her surroundings (for example, "being in a daze")
   3. derealization
   4. depersonalization
   5. dissociative amnesia (that is, inability to recall an important aspect of the trauma)

C. The traumatic event is persistently reexperienced in at least one of the following ways:
   1. recurrent images, thoughts, dreams, illusions, flashback episodes, or a sense of reliving the experience
   2. distress on exposure to reminders of the event.

D. Marked avoidance of stimuli that arouse recollections of the trauma (for example, thoughts, feelings, conversations, activities, places, people).

E. Marked symptoms of anxiety or increased arousal (for example, difficulty sleeping, irritability, poor concentration, hypervigilance, exaggerated startle response, motor restlessness).

F. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning, or impairs ability to pursue some necessary task such as obtaining assistance or mobilizing personal resources by telling family members about the traumatic experience.

G. The disturbance lasts for a minimum of 2 days and a maximum of 4 weeks and occurs within 4 weeks of the traumatic event.

H. The disturbance is not due to the direct physiological effects of a substance (for example, a drug of abuse, a medication) or a general medical condition, is not better accounted for by Brief Psychotic Disorder, and is not merely an exacerbation of a preexisting Axis I or Axis II disorder.

** Adapted from DSM-IV, American Psychiatric Association*

Table 6. Diagnostic criteria for posttraumatic stress disorder*

A. The person has been exposed to a traumatic event characterized by both of the following:
   1. actual or threatened death or serious injury, or a threat to the physical integrity of self or others
   2. a response of intense fear, helplessness, or horror (in children, this may be expressed by disorganized or agitated behavior)

B. The traumatic event is persistently reexperienced in one or more of the following ways:
   1. recurrent or intrusive distressing recollections of the event, including images, thoughts, or perceptions (in young children, repetitive play may occur in which themes or aspects of the trauma are expressed)
   2. recurrent distressing dreams of the event (in children, there may be frightening dreams without recognizable content)
   3. acting or feeling as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations, and dissociative flashback episodes, including those that occur on awakening or when intoxicated); in young children, trauma-specific reenactment may occur.
   4. intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event
   5. physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event

C. Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three or more of the following:
   1. efforts to avoid thoughts, feelings, or conversations associated with the trauma
   2. efforts to avoid activities, places, or people that arouse recollections of the trauma
   3. inability to recall an important aspect of the trauma
   4. markedly diminished interest or participation in significant activities
   5. feeling of detachment or estrangement from others
   6. restricted range of affect (e.g., unable to have loving feelings)
   7. sense of foreshortened future (no expectation of career, marriage, children, or a normal life span)

D. Persistent symptoms of increased arousal (not present before the trauma), as indicated by two or more of the following:
   1. difficulty falling or staying asleep
   2. irritability or outbursts of anger
   3. difficulty concentrating
   4. hypervigilance
   5. exaggerated startle response

E. Duration of the disturbance (symptoms in Criteria B, C, and D) for more than 1 month.

F. The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Specify if: *Acute* (symptoms for less than three months); *Chronic* (symptoms for 3 months or more); or *With Delayed Onset* (symptoms begin at least 6 months after the stressor).

**Adapted from DSM-IV, American Psychiatric Association*

US Antiterrorism and Effective Death Penalty Act. This act regulates commerce in and the transfer of listed biological agents. In 1997, Congress enacted the Defense Against Weapons of Mass Destruction Act and amended the Defense Authorization Act to strengthen the federal government's ability to prevent and respond to bioterrorist incidents, support state and local prevention and response efforts, and improve state and local emergency capabilities. Congress recently appropriated funds to assess the risks associated with specific agents and for development of additional coordinated federal, state and local response capacities.[4,7,24,25]

In the event of a domestic bioterrorist event, the DOD can provide technical assistance, bomb disposal, decontamination, security, and other services.[24] The DOD already has an ambitious program of defense against BW and domestic

bioterrorism, which includes improving surveillance and intelligence systems; developing vaccines, antitoxins, and antimicrobial prophylaxis and therapeutic protocols; developing sensitive and specific ways to detect and isolate biological agents; improving protective clothing and other protective devices; and training decontamination teams, triage personnel and field commanders.[7,26] Since 1997, the DOD has expanded the preparedness and response capabilities of local, state and federal agencies by training and equipping fire, police, rescue, and hospital emergency department personnel in over 100 US cities.[7,24] In addition, the US Marine Corps has a Chemical/Biological Incident Response Force (CBIRF), comprised of 350 Marines, Navy and support personnel. From its base at Indian Head, MD, this unit can respond to incidents of bioterrorism at home or in US facilities abroad.

The medical, psychosocial, and economic impact of a bioterrorist attack will depend on the agent or toxin used, the method and efficacy of its dispersal, the population exposed, the level of immunity in the population, the availability of effective postexposure prophylaxis, and the potential for secondary transmission. The speed with which a post-attack intervention program can be implemented is critically important, particularly when the agents involved have short incubation periods or rapid onset of action. Delay in starting prophylaxis or treatment is the single most important element leading to increased morbidity, mortality and costs,[13] but early recognition of a bioterrorist event depends on sensitive epidemiologic surveillance and a high index of suspicion on the part of health care providers who evaluate the initial cases. Following recognition, the goals of management are rapid and accurate identification of the agent involved, careful assessment of exposure, appropriate triage and quarantine, and effective treatment or immunization.[6,17] With some agents, active or passive postexposure immunization and prophylactic treatment with antimicrobial drugs may ameliorate symptoms and prevent or reduce the severity of clinical illness. Once a victim has become ill, medical personnel must institute agent-specific therapies and supportive care.[8]

"Assessment of the symptoms associated with specific biological agents and familiarity with specific epidemiological variables may help to distinguish natural from intentional disease outbreaks."

Assessment of the symptoms associated with specific biological agents and familiarity with specific epidemiological variables may help to distinguish natural from intentional disease outbreaks. Detailed articles on the clinical assessment and medical management of patients exposed to biological warfare agents are available.[4,8,10,26-28] The DHHS, through the Centers for Disease Control and Prevention (CDC), is upgrading national, state, and local capabilities with a five-part program: 1) Preparedness Planning and Readiness Assessment, 2) Surveillance and Epidemiology Capacity, 3) Laboratory Capacity-Biological Agents, 4) Laboratory Capacity-Chemical Agents, and 5) Health Alert Network/Training. The CDC already collaborates with states in infectious disease surveillance, laboratory diagnosis, and epidemiologic support. The CDC has demonstrated effective communication with state public health agencies (in response to a series of anthrax-related threats) and has begun to educate health professionals on the public health dimensions of bioterrorism.[28-30]

When bioterrorism threats or acts occur, the local emergency response system should be activated by dialing 911 if that system is in use, or by notifying local law enforcement authorities. Local and state public health authorities and the local FBI field office also should be notified.[28] Clinicians whose patients have symptoms or illness compatible with exposure to bioterrorist agents should contact local and state public health authorities and consult infectious disease and toxin experts at academic medical centers, the CDC and the USAMRIID (see Table 4).

Adverse Mental Health Effects-Acute Stress Disorder and Posttraumatic Stress Disorder

Terrorism is a form of psychological warfare. It uses violence or the threat of violence to achieve political, religious, or ideological objectives. Terrorists select targets with maximum shock value, and they measure the ultimate success of their activities not only by number of casualties but also—and perhaps even more importantly—by the psychological effect on the whole target population.[23] The novelty of biological weapons and our deeply rooted fears of them means that there will be strong psychological and physiological responses to bioterrorist attacks.[17] There will be psychological fallout among survivors, emergency workers and those investigating an incident or containing a threat.

The first stress induced by a bioterrorist attack is the threat (and actuality) of infection. First responders, laboratory workers, emergency medical and primary care providers, epidemiologists, and pathologists are especially at risk. Fear of illness or death may lead some personnel to flee the affected area unless they are confident they can protect themselves.[17] Health care systems may be overwhelmed by the numbers of people seeking help; health care providers may need physical protection from those demanding treatment, particularly if prophylactic or therapeutic agents are scarce. The mental health of emergency workers and medical

personnel will have to be closely monitored, and we will need contingency plans for dealing with public hysteria and the disruption of health care delivery.[8,12]

Unfortunately, most medical personnel are not trained to work in protective clothing or while using protective equipment such as respirators. Studies by the military show that use of protective clothing and other apparatus in disaster settings causes anxiety, claustrophobia, difficulties with breathing apparatus, overheating, dehydration, and failure to recognize danger.[1,31,32] During simulated chemical or biological warfare, 10-20% of participants experienced moderate to severe psychological symptoms and 4-10% actually had to stop the exercise because of claustrophobia, anxiety or panic, or difficulty with protective gear.[31,32] The implications are ominous for civilian health workers, who have little or no training in performing under such conditions.

Following the report of an attack, both exposed and unexposed people may experience acute anxiety due to autonomic arousal (muscle tension, tachycardia, hyperventilation, sweating, tremor, and a sense of foreboding). These symptoms may be misattributed to the bioterrorist agent. However, because many agents can cause mental dysfunction, a careful mental status examination will be required to differentiate agent-induced disorders of mood, behavior, and cognition from psychiatric disorders. Other psychological responses include horror, anger, panic, magical thinking about microbes, attribution of arousal symptoms to infection, fear of invisible agents, fear of contagion, anger at terrorists (or the government), scapegoating, paranoia, social isolation, demoralization, feelings of helplessness and hopelessness, and loss of faith in social structure.[17] Large numbers of casualties may induce panic, public hysteria and social disorder, which further disrupt health care delivery systems.[4,17]

Substantial research indicates that the mental health of emergency and first response workers, hospital-based medical personnel, and the public can be acutely and chronically affected by terrorist acts and disasters. The literature focuses on acute stress disorder (ASD) and posttraumatic stress disorder (PTSD),[17,23,34,35] for which Tables 5 and 6 (pages 156-7) outline the diagnostic criteria. These disorders manifest by flashbacks, nightmares, sleep disorders, eating disturbances, fatigue, difficulty concentrating, guilt, hypervigilance, anxiety, depressed mood, loss of libido, irritability, and social conflict. In a bioterrorism crisis, ASD and PTSD may arise from the stress of dealing with large numbers of deaths, watching one's co-workers, friends and loved ones die, the quarantine of family members or entire communities, and dealing with dead bodies (the more gruesome and slow the death, the worse the psychological sequelae). Some victims cannot come to terms with acts of terrorism unless they get external support; feelings of despair and hopelessness can lead to suicide.[17,36]

The psychological morbidity of terrorist attacks is quite high, including depression and pathological bereavement as well as ASD and PTSD.[36] A study of adult survivors of the Oklahoma City bombing indicates that 34% of 182 survivors studied developed PTSD and another 11%, other psychiatric illness (depression or substance abuse).[38] Fortunately, most people exposed to disasters and other traumatic events have no prolonged psychological sequelae,[23] but those with previous trauma, those without social supports, and first responders (police and emergency medical personnel) are at high risk.[15,17,25,27] The very nature of bioterrorism probably puts all personnel involved in trying to identify and contain the agent at high risk for psychiatric sequelae.

People report different symptoms depending on how much time has elapsed since the traumatic event. During the emergency phase (1-3 weeks after the event) survivors are preoccupied with thoughts about it and openly express their anxieties. During the inhibition phase (3-6 weeks after the event), survivors commonly experience social conflict, disturbed dreams and other health problems. The adaptation phase (6 or more weeks after the event) is characterized by remission of most signs of distress.[23]

Other Stress-Associated Sequelae

A number of studies about the sequelae of man-made and natural disasters may be pertinent to bioterrorism. The more we learn about how people cope, the better health professionals can prepare for and respond to the devastation of terrorism. In addition to ASD, PTSD, depression, and even suicide, epidemiologic studies indicate that war or natural disasters exacerbate chronic diseases such as asthma, hypertension, coronary artery disease, diabetes mellitus, peptic ulcer disease, and seizure disorder.* Some studies show a direct relationship between morbidity and mortality and the degree of devastation, loss of family and loved ones, loss of property, or relocation to unfamiliar areas. We can predict that bioterrorist events will increase the incidence of stroke, myocardial infarction, bleeding ulcers, and the medical sequelae of common chronic diseases. These events will complicate triage, particularly early in the crisis, and further stress the health care delivery system.[17]

Mental Health, Psychiatric, and Social Interventions

The primary goal of psychiatric evaluation is to assess how well survivors and especially first responders and health care personnel cope with and adapt to stress. Psychiatric intervention may also help in other ways, including the prevention of

*Additional references are listed separately at the end of this article.

group panic, careful and rapid medical evaluation and treatment, the avoidance of emotional responses such as "knee-jerk" quarantine, effective communication about risk, control of symptomatic hyperarousal (via reassurance and use of pharmacological anxiolytics as necessary), management of anger and fear, clarification of misattributed somatic symptoms, treatment of depression and suicidal ideation, provision of respite as required, and restoration of those suffering mental sequelae to effective, useful social roles in the community.[17] Social support is quite important. Friends, neighbors and colleagues can help bolster coping efficacy, and the mental, emotional and spiritual bonding that occurs within communities can overcome the trauma of terrorist bombings. The psychological value of "pulling together" within the community and the involvement of social support systems such as organized religion should not be underemphasized.[23,39] Maintaining contact with parents is especially important for children; family members should not be separated from one another if possible. If quarantine or isolation is necessary to prevent spread of infection, telecommunications (telephones, televisions, the Internet) can help prevent social isolation and a sense of stigmatization.[17]

The medical community has long recognized the value of early psychological intervention and counseling for victims of natural and man-made disasters. The Critical Incident Stress Management (CISM) program uses Critical Incident Stress Debriefing (CISD) to prevent or mitigate adverse psychological reactions in emergency and public safety personnel, physicians, nurses, and disaster management and relief personnel.[17,23,40-43] One facet of preparedness is the development of CISM programs and identification of CISD teams to focus on the unique psychological issues associated with bioterrorism. Given the potential need for quarantine or isolation after bioterrorist events, it may be helpful to develop "teledebriefing" capability (similar to the use of telemedicine in disasters [44]) for mental health professionals who cannot safely be brought into physical proximity with victims.[17]

Bioterrorism requires new classes of emergency response personnel. Teams trained to deal with man-made accidents and disasters involving the release of radiation, pesticides, and hazardous materials already exist in many states. However, these teams are not currently trained or adequately equipped to respond to the purposeful release of chemical and biological agents. Given the inevitable delays in deploying federal response units, it is important that local and state agencies develop specially-trained chemical agent and biohazard first-responder teams. As part of the Domestic Preparedness Program, DOD has begun such training for traditional first responders, and the PHS has established 24-hour on-call metropolitan medical strike teams (which include mental health professionals) in the nation's 120 largest cities.[24] Like their federal counterparts, these teams focus on technical assessment and management of the problem at hand, and, in collaboration with traditional first responders, they place primary emphasis on rescue and recovery, triage and prehospital treatment of the sick and injured, maintenance of public safety, and protection of property and the environment. Deployment of specialized teams will reduce the potential for psychological stress in first responders.

The effects of a terrorist release of a microbiologic agent (in contrast to a toxic gas) are usually not evident for several days, so traditional first responders may have only a limited role. It is more likely that medical personnel in emergency rooms, primary care physicians, and infectious disease specialists will be the unwitting "first responders," and may find themselves exposed--even dying--before the infectious agent is recognized. This means we will have to make a major commitment to improve and integrate epidemiologic surveillance systems at the local, state and federal levels, and educate all health workers so that they are aware of the threat.

"Given the inevitable delays in deploying federal response units, it is important that local and state agencies develop specially-trained chemical agent and biohazard first-responder teams."

Discussion and Summary

During World War II, the US government commissioned Norman Rockwell to paint a series of pictures depicting "The Four Freedoms"– Freedom of Speech, Freedom of Religion, Freedom from Want, and Freedom from Fear. Terrorism violates our right to be free from fear.[45] Today, a seemingly endless series of highly publicized mass killings in the workplace, schools, abortion clinics, and elsewhere fosters a growing concern about acts of terrorism. Governments and the medical profession must take steps to prevent terrorist acts and, if that effort fails, to minimize the health consequences of such acts and bring the perpetrators to justice.

The psychological issues related to terrorism include both the mind-set of the perpetrators and the psychological responses of victims and the public. The victims and the general public may have underlying psychiatric conditions aggravated or rekindled in response to a terrorist attack; otherwise psychologically healthy persons may experience *de novo* psychiatric symptoms such as anxiety, fear, hysteria or panic. Often, the perpetrators are mentally ill, and may have previously sought psychiatric treatment. Usually, their stated motivation is revenge for real or imaginary wrongs.

The threat of terrorist acts has increased efforts to have mental health and other professionals identify and report

persons with fantasies of or plans for violent assaults. The Tarasoff decision[46] on "duty to warn" made mental health professionals aware that "where public peril begins, individual privilege of medical confidentiality ends." Since the 1970s, the forced hospitalization and treatment of mentally ill persons perceived to pose a risk of violence has been complicated by the strict legal standard of "clear and immediate danger to oneself or the public" as a necessary criterion for commitment. While most jurisdictions allow some flexibility, it can still be difficult to keep a person hospitalized involuntarily. Sometimes the seriously mentally ill are dangerous only if they discontinue taking psychotropic medication, or if they have access to alcohol or other drugs. This means the period of clear and immediate danger may be brief and rapidly correctable. However, some of those hospitalized for treatment will, on release, discontinue their medications or again abuse intoxicating drugs. In many states there is no way to treat these patients without their consent, but efforts are underway to address these and other problems through laws permitting commitment and conditional release.

Increased concern about BW and domestic bioterrorism coincides with a decline in cold war fears of international nuclear mass annihilation. We do not know how much stress was experienced by populations subjected to the threat of nuclear holocaust, but it was probably tempered by the protracted nature of the risk, the lengthy discussions about disarmament, and the conclusion that individuals were powerless to alter the course of international events. The threat of nuclear terrorism still exists, and we can learn something from the global experience. At the beginning of the cold war, except for vivid accounts of death and destruction in Hiroshima and Nagasaki, the general public was largely ignorant about nuclear war and the acute and chronic health effects of ionizing radiation. Subsequent scientific inquiry by the Atomic Bomb Casualty Commission and others helped define the health risks and hazards of nuclear war, and helped shape policy decisions about national and international preparedness, deterrence and disarmament.

BW is not new. What is new is the likelihood that biological, not nuclear, agents will be used both in conventional wars and in acts of domestic and international terrorism. The technology is just too simple and accessible. The psychological issues related to bioterrorism hinge on the public's abiding fear of infection and its ignorance of biomedical issues. The best way to deal with this is a concerted campaign to educate the public about bioterrorism and what governments and other agencies are doing in terms of prevention, preparedness and response. The media can play an active role by educating the public about the health threats of bioterrorism.[17]

Psychiatry has three professional roles regarding bioterrorism. The first is primary prevention. Psychiatrists can develop psychological profiles to identify individuals and organizations at risk to initiate or participate in terrorist activities. These include some people with untreated paranoid schizophrenia, xenophobics, religious fanatics and zealots, members of cults or racial and ethnic hate organizations, radical antiabortionists and environmentalists (self-proclaimed "eco-terrorists"), and those spouting anti-government or ultra-nationalistic rhetoric. Psychiatrists, psychologists, and other mental health care providers should respond to persons who make terrorist threats in the same way that pediatricians and social workers respond to threats of child abuse, and the way teachers, classmates, parents, and health care providers respond to threats of gun-related violence by disturbed students. Bioterrorism threatens national security and the public health, and its prevention must take precedence over patient confidentiality and the personal freedoms of would-be criminals. We can only wonder whether those arrested for ordering *Y. pestis* or for possessing ricin and botulinum toxins communicated clues about their intentions to family, neighbors, friends, or health care providers. In any case, states need to pass laws protecting medical professionals from civil and criminal liability when they report conversations, threats, or activities related to terrorism or other forms of violence. We already have such legislation regarding child abuse, communicable diseases, and illnesses due to occupational and environmental hazards. None of these poses as catastrophic a threat to public health as bioterrorism does.

"Psychiatrists, psychologists, and other mental health care providers should respond to persons who make terrorist threats in the same way that pediatricians and social workers respond to threats of child abuse …"

Secondly, mental health care providers should be prepared to serve in emergency roles if needed. They should participate in local, state, and national planning and preparedness activities, including disaster drills involving bioterrorism. In the event of an actual bioterrorist event, psychiatrists will have to use their knowledge and skills to assess the efficacy of coping and adaptation by survivors and rescue personnel, especially first responders and health care workers. Psychiatric interventions, particularly those associated with CISM and CISD, will play a pivotal role in maintaining and restoring normal mental health functioning after a bioterrorist attack.

Thirdly, mental health professionals and agencies should prepare to deal with the psychosocial aftermath of bioterrorism. They should be familiar with the diagnostic criteria for Acute Stress Disorder (Table 5) and Postraumatic

Stress Disorder (Table 6) and the Critical Incident Stress Management (CISM) and Critical Incident Stress Debriefing (CISD) interventions used in post-disaster settings. Information about these topics should be reviewed regularly, and educational update programs offered on a regular basis. Understanding the potential medical and psychosocial sequelae discussed in this paper and elsewhere can provide a solid foundation for an organized and effective medical and mental health response capability.

Despite the growing concern about bioterrorism, we know little about its nature. There never has been a major attack, and so there is no track-record with which to determine how best to respond. We are today where we were 30 years ago with respect to conventional terrorism. A bioterrorist attack could create a medical, political, and social catastrophe unparalleled in history. It might even mean the imposition of martial law by the President. The greatest payoff will come from a well-organized response to an incident.[4] Consequently, we must have an effective plan for the early involvement of psychiatrists, psychologists and other mental health professionals at the local, state, and national levels.

We should keep the concept of "dual use" at the forefront as we develop multidisciplinary and interdisciplinary efforts to combat bioterrorism, and as we enhance surveillance, epidemiological, laboratory and other capacities. In 1951, the CDC created the Epidemic Intelligence Service, staffed by epidemiologists trained to respond in case of a BW attack in the US. This was doubly sensible because the sound epidemiologic investigation of disease outbreaks, whether natural or purposeful, provides big public health dividends.[8] Efforts under way in North Carolina and elsewhere to develop an enhanced public health and mental health response to the threat of bioterrorism will lead to capabilities that will be helpful in conventional terrorism and the many other natural and man-made disasters that the future holds.

Disclaimer: The opinions expressed are those of the authors and and should not be interpreted as those of the NC Department of Health and Human Services, the University of North Carolina, or the North Carolina Medical Society.

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